# CLAIMS

What is claimed is:

1. An aseptic fluidic interface apparatus between bioprocess systems, comprising:
   an inlet valve, adapted for automatic control, coupled to a biofluid source site;
   a sampling conduit extending from the inlet valve to an outlet valve adapted for automatic control, wherein the outlet valve is coupled to a biofluid process site;
   a trap at the sampling conduit;
   a waste valve, adapted for automatic control, that is located at a waste conduit extending from the sampling conduit to a waste site; and
   a wash fluid source coupled to at least one of the inlet or outlet valves.

2. The apparatus of Claim 1, further comprising an automated controller that controls the valves to aseptically collect biofluid samples from the source site and direct the samples to the process site.

3. The apparatus of Claim 2, wherein the automated controller collects a biofluid sample by opening the inlet valve and outlet valves and closing the waste valve.

4. The apparatus of Claim 3, wherein the automated controller isolates the biofluid sites by closing the inlet and outlet valves.

5. The apparatus of Claim 4, wherein the automated controller isolates the biofluid sites by opening the waste valve to drain biofluid to the waste site from the trap.

6. The apparatus of Claim 5, wherein the automated controller cleans the sampling conduit before sample collection by directing a wash fluid through at least one valve selected from the inlet and outlet valves, and subsequently through the waste valve to the waste site.

7. The apparatus of Claim 2, wherein the lowest portion of the trap is located below the inlet or the outlet valve by a distance at least about 3 times the inside diameter of the conduit.

8. The apparatus of Claim 7, wherein the inlet and the outlet valves are located at the same height.

9. The apparatus of Claim 8, wherein the waste valve is coupled to the lowest point of the trap.

10. The apparatus of Claim 9, wherein the enclosed volume of the conduits bounded by the valves, in milliliters, is less than about 10 times the cross sectional area of the conduit in millimeters$^2$.

11. The apparatus of Claim 2, further comprising a flow sensor, in electronic communication with the automated controller, that is located between the trap and the waste site and senses fluid transiting the inlet or outlet valve.

12. The apparatus of Claim 2, further comprising a relief valve located at an relief conduit, wherein the proximal end of the relief conduit is coupled to the waste conduit between the trap and the waste valve, and the distal end is in fluid communication with the external environment.

13. The apparatus of Claim 12, further comprising a filter located at the relief conduit that excludes at least a portion of external contaminants from at least a portion of the relief conduit.

14. The apparatus of Claim 13, wherein the filter is selected to exclude contaminants greater than about 0.2 $\mu$m in diameter.

15. The apparatus of Claim 14, wherein the filter is located at the distal end of the relief conduit, further comprising an overflow reservoir to collect overflow fluid that is located at the relief conduit between the relief valve and the filter.

16. The apparatus of Claim 15, further comprising a flow sensor located at the relief conduit between the relief valve and the overflow reservoir.

17. The apparatus of Claim 15, further comprising a second filter, located at the relief conduit between the relief valve and the overflow reservoir, that is selected to exclude contaminants greater than about 0.2 $\mu$m in diameter.

18. The apparatus of Claim 2, wherein the automated controller directs the wash fluid through the outlet valve into the sampling conduit.

19. The apparatus of Claim 18, wherein the wash fluid comprises a sterile fluid selected from steam, compressed air, an organic solvent, supercritical $CO_2$, and an aqueous cleaning solution.

20. The apparatus of Claim 19, wherein the automated controller directs the wash fluid from the sampling conduit through the input valve to the biofluid source site.

21. The apparatus of Claim 19, wherein the automated controller directs the wash fluid from the sampling conduit through the waste valve to the waste site.

22. The apparatus of Claim 19, further comprising at least one double isolated gate valve among the inlet and outlet valves, an output of at least one double isolated gate valve being coupled to the waste site.

23. The apparatus of Claim 22, further comprising the automated controller directing the wash fluid through at least one double isolated gate valve to the waste site.

24. The apparatus of Claim 23, wherein the inlet and outlet valve are each a double isolated gate valve.

25. An aseptic fluidic interface between bioprocess systems, comprising:

an inlet valve coupled to a biofluid source site, the inlet valve being a double isolated gate valve that has a first output coupled to a waste site;

a sampling conduit extending from a second output of the inlet valve to an outlet valve, the sampling conduit having a trap at a height lower than the inlet and outlet valves, the outlet valve being a double isolated gate valve having a second input coupled to a wash fluid source, and the outlet valve coupled to a biofluid process site at the same height as the inlet valve;

a waste valve at a waste conduit extending from the bottom of the trap to the waste site;

a relief conduit extending from the waste conduit between the trap and the waste valve to an overflow filter, the filter selected to exclude particulate contaminants greater than about 0.2 $\mu$m in diameter;

at the relief conduit, a relief valve between the trap and the filter; an overflow reservoir between the relief valve and the filter; and a flow sensor between the relief valve and the overflow reservoir;

an automated controller in communication with the valves and the sensor that:

collects a biofluid sample by opening the inlet and outlet valves and closing the waste and relief valves, directing a sample from the source site to the process site;

isolates the biofluid sites by closing the inlet and outlet valves; and alternately:

opening the waste valve to drain biofluid from the trap to the waste site and closing the relief valve; and

opening the relief valve, closing the waste valve, and sensing biofluid draining from the trap to the overflow reservoir; and

cleans the sampling conduit before each sample collection by directing wash fluid through the outlet valve into the sampling conduit, and subsequently to the waste site alternately through the first output of the inlet valve and the waste valve.

26. A method of aseptically sampling a biofluid, comprising automatically:

collecting a biofluid sample by opening an inlet valve at a biofluid source site;

directing the sample to a biofluid process site by opening an outlet valve coupled to the process site, and closing a waste valve that couples a trap and a waste site, wherein the trap is located at a sampling conduit extending from the inlet valve to the outlet valve;

isolating the biofluid sites by:

closing the inlet and outlet valves;

opening the waste valve to drain biofluid from the trap to the waste site;

cleaning the sampling conduit before sample collection by directing a wash fluid through at least one valve selected from the inlet and outlet valves, and subsequently through the waste valve to the waste site.

27. The method of Claim 26, further comprising cleaning before collecting each sample.

28. The method of Claim 27, further comprising cleaning to reduce the number of bacterial colony forming units per milliliter of rinse water to less than about 100.

29. The method of Claim 27, further comprising cleaning to reduce macromolecule contamination in rinse water to less than about 1 part per million.

30. The method of Claim 27, further comprising cleaning by directing wash fluid through the outlet valve into the sampling conduit.

31. The method of Claim 30, further comprising employing a wash fluid selected from steam, compressed air, an organic solvent, supercritical $CO_2$, and an aqueous cleaning solution.

32. The method of Claim 31, further comprising directing the wash fluid through the input valve to the biofluid source site.

33. The method of Claim 32, further comprising directing the wash fluid through a double isolated gate valve to the waste site, at least one of the inlet and outlet valves being a double isolated gate valve, an output of each double isolated gate valve being coupled to the waste site.

34. The method of Claim 33, wherein the inlet valve is a double isolated gate valve.

35. The method of Claim 33, wherein the outlet valve is a double isolated gate valve.

36. The method of Claim 26, further comprising monitoring for a backflow condition while the biofluid sites are isolated by sensing fluid flow.

37. The method of Claim 36, further comprising sensing for fluid flow in the sampling conduit.

38. The method of Claim 36, further comprising sensing for fluid flow through the waste valve.

39. The method of Claim 36, further comprising isolating the biofluid sites by closing the waste valve and opening a relief valve that is located at a relief conduit, wherein the relief conduit has a proximal end coupled to the trap and a distal end coupled to the external environment.

40. The method of Claim 39, further comprising sensing for fluid flow in the relief conduit.

41. The method of Claim 40, further comprising excluding particulate contaminants from entering the relief conduit by employing a filter selected to remove particulates having a diameter of at least about .2 $\mu$m.

42. The method of Claim 41, further comprising collecting overflowing biofluid in an overflow reservoir at the relief conduit.

43. The method of Claim 26, further comprising locating the inlet and outlet valves at the same height.

44. The method of Claim 43, further comprising draining biofluid from the trap at a location that is lower than the inlet and the outlet valves by at least about 3 times the inside diameter of the conduit.

45. The method of Claim 44, further comprising draining biofluid from the lowest point of the trap.

46. A method of aseptically sampling a biofluid, comprising automatically:

collecting a biofluid sample by opening an inlet valve at a biofluid source site;

directing the sample to a biofluid process site by:

opening an outlet valve, coupled to the process site, that is located at the same height as the inlet valve;

closing a waste valve that couples a trap and a waste site, wherein the trap is located at a sampling conduit extending from the inlet valve to the outlet valve;

isolating the biofluid sites by:

closing the inlet and outlet valves;

opening the waste valve to drain biofluid from the trap to the waste site;

closing the waste valve and opening a relief valve located at a relief conduit, wherein the relief conduit has a proximal end coupled to the trap and a distal end coupled to a filter selected to exclude particulate contaminants having a diameter of at least about .2 um;

monitoring for backflow by sensing fluid flow in the relief conduit

cleaning the sampling conduit before collecting each sample, including:

directing a wash fluid through the outlet valve, into the sampling conduit, and through the waste valve to the waste site; and

reducing macromolecule contamination in the sampling conduit to less than about 1 part per million.

47. An apparatus for aseptically sampling a biofluid, comprising:

means for automatically collecting a biofluid sample from a biofluid source site and directing the sample to a biofluid process site;

means for automatically isolating the biofluid sites; and

means for automatically cleaning the apparatus.

48. An apparatus for automated aseptic sampling and preparation of a macromolecule from a bioreactor, comprising:

an inlet valve coupled to a biofluid source site;

a sampling conduit extending from the inlet valve to an outlet valve that is coupled to a rough separation circuit;

a trap located at the sampling conduit;

a waste valve at a waste conduit that extends from the sampling conduit to a waste site;

a wash fluid source coupled to at least one of the inlet or outlet valves;

a rough separation circuit comprising a rough pump, a first stage rough filter selected to separate rough components, and a second stage rough filter selected to separate rough components that pass through the first stage rough filter;

a fine/desalination circuit, comprising a fine pump, a reservoir that supplies a desalination buffer, and a fine filter s selected to separate fine components from the macromolecule; and

a denaturation circuit comprising a denaturation pump, a denaturing vessel comprising a heating element and a cooling element, a precipitation pump, a reservoir supplying a denaturation buffer, a reservoir supplying a pH buffer, a pH sensor and a precipitation filter selected to separate insoluble denaturation precipitate components; and

an automated controller that is in electronic communication with the valves, the pumps, the sensors, the heating element and the cooling element.